Patent

**Amendments to the Claims:** 

This listing of claims will replace all prior versions, and listings, of claims in the

application:

**Listing of Claims:** 

Claims 1 to 149 (Canceled).

150. (New) A method of treating a subject with a B-cell malignancy, the method comprising

administering to the subject a therapeutically effective dose of a composition comprising a

monomeric cytotoxic drug derivative/anti-CD22 antibody conjugate, wherein the anti-CD22

antibody of the monomeric cytotoxic drug derivative/anti-CD22 antibody conjugate comprises a

light chain variable region having a sequence set forth in SEQ ID NO:19 and a heavy chain

variable region having a sequence set forth in SEQ ID NO:27.

151. (New) The method of claim 150, wherein the anti-CD22 antibody is selected from a

group consisting of a monoclonal antibody, a chimeric antibody, a human antibody, a

humanized antibody, a single chain antibody, and a biologically active antibody fragment

wherein the biologically active fragment is a Fab, a modified Fab, Fab', F(ab')2 or Fv, or a heavy

chain monomer or dimer.

152. (New) The method of claim 151, wherein the anti-CD22 antibody is a humanized

antibody.

153. (New) The method of claim 152, wherein the humanized antibody comprises a variable

domain comprising human acceptor framework regions and non-human donor CDRs.

154. (New) The method of claim 153, wherein the human acceptor framework regions of the

variable domain of the heavy chain of the antibody are based on SEQ ID NOS:21 and 22 and

comprise donor residues at positions 1, 28, 48, 72 and 97 in SEQ ID NO:8.

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155. (New) The method of claim 154, wherein the antibody further comprises donor residues

at positions 68 and 70 in SEQ ID NO:8.

156. (New) The method of claim 152, wherein the anti-CD22 antibody comprises a variable

domain of the light chain comprising a human acceptor framework region based on SEQ ID

NOS:17 and 18 and further comprising donor residues at positions 2, 4, 42, 43, 50 and 65.

157. (New) The method of claim 156, wherein the anti-CD22 antibody further comprises a

donor residue at position 3 in SEQ ID NO:7.

158. (New) The method of claim 150, wherein the cytotoxic drug is calicheamicin.

159. (New) The method of claim 158, wherein the calicheamicin is gamma calicheamicin or

N-acetyl gamma calicheamicin.

160. (New) The method of claim 158, wherein the calicheamicin derivative is functionalized

with 3-mercapto-3-methyl butanoyl hydrazide.

161. (New) The method of claim 150, wherein the therapeutically effective dose of the

composition is administered subcutaneously, intraperitoneally, intravenously, intraarterially,

intramedullarly, intrathecally, transdermally, transcutaneously, intranasally, topically, enterally,

intravaginally, sublingually or rectally.

162. (New) The method of claim 161, wherein the therapeutically effective dose of the

composition is administered intravenously.

163. (New) The method of claim 150, wherein the subject is a human subject.

164. (New) The method of claim 150, wherein the B-cell malignancy is a leukemia, a

lymphoma or a Non-Hodgkin's lymphoma.

165. (New) The method of claim 164, wherein the leukemia expresses cell surface antigen

CD22.

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166. (New) The method of claim 164, wherein the lymphoma expresses cell surface antigen

CD22.

167. (New) The method of claim 150, comprising administering the therapeutically effective

dose of the composition with one or more bioactive agents.

168. (New) The method of claim 167, wherein the one or more bioactive agents are

antibodies.

169. (New) The method of claim 168, wherein the antibody is directed against a cell surface

antigen expressed on B-cell malignancies.

170. (New) The method of claim 169, wherein the antibody directed against cell surface

antigens expressed on B-cell malignancies is selected from a group consisting of anti-CD19,

anti-CD20 and anti-CD33 antibodies.

171. (New) The method of claim 170, wherein the anti-CD20 antibody is rituximab.

172. (New) The method of claim 168, wherein the therapeutically effective dose of the

composition is administered together with an antibody directed against a cell surface antigen on

B-cell malignancies, and optionally comprising one or more combinations of cytotoxic agents as

a part of a treatment regimen, wherein the combination of cytotoxic agents is selected from:

A. CHOPP (cyclophosphamide, doxorubicin, vincristine, prednisone, and procarbazine);

B. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone);

C. COP (cyclophosphamide, vincristine, and prednisone);

D. CAP-BOP (cyclophosphamide, doxorubicin, procarbazine, bleomycin, vincristine, and

prednisone);

E. m-BACOD (methotrexate, bleomycin, doxorubicin, cyclophosphamide, vincristine,

dexamethasone, and leucovorin);

F. ProMACE-MOPP (prednisone, methotrexate, doxorubicin, cyclophosphamide,

etoposide, leucovorin, mechloethamine, vincristine, prednisone, and procarbazine);

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- G. ProMACE-CytaBOM (prednisone, methotrexate, doxorubicin, cyclophosphamide, etoposide, leucovorin, cytarabine, bleomycin, and vincristine);
- H. MACOP-B (methotrexate, doxorubicin, cyclophosphamide, vincristine, fixed dose prednisone, bleomycin, and leucovorin);
- MOPP (mechloethamine, vincristine, prednisone, and procarbazine);
- J. ABVD (adriamycin/doxorubicin, bleomycin, vinblastine, and dacarbazine);
- K. MOPP (mechloethamine, vincristine, prednisone, and procarbazine) alternating with ABV (adriamycin/doxorubicin, bleomycin, and vinblastine);
- L. MOPP(mechloethamine, vincristine, prednisone, and procarbazine) alternating with ABVD (adriamycin/doxorubicin, bleomycin, vinblastine, and dacarbazine);
- M. ChIVPP (chlorambucil, vinblastine, procarbazine, and prednisone);
- N. IMVP-16 (ifosfamide, methotrexate, and etoposide);
- O. MIME (methyl-gag, ifosfamide, methotrexate, and etoposide);
- P. DHAP (dexamethasone, high-dose cytarabine and cisplatin);
- Q. ESHAP (etoposide, methylpredisolone, high-dose cytarabine, and cisplatin);
- R. CEPP(B) (cyclophosphamide, etoposide, procarbazine, prednisone, and bleomycin);
- S. CAMP (lomustine, mitoxantrone, cytarabine, and prednisone);
- T. CVP-1 (cyclophosphamide, vincristine, and prednisone). ESHOP (etoposide, methylpredisolone, high-dose cytarabine, vincristine and cisplatin);
- U. ESHOP (etoposide, methylpredisolone, high-dose cytarabine, vincristine and cisplatin);
- V. EPOCH (etoposide, vincristine, and doxorubicin for 96 hours with bolus doses of cyclophosphamide and oral prednisone);
- W. ICE (ifosfamide, cyclophosphamide, and etoposide);
- X. CEPP(B) (cyclophosphamide, etoposide, procarbazine, prednisone, and bleomycin);
- Y. CHOP-B. (cyclophosphamide, doxorubicin, vincristine, prednisone, and bleomycin); and
- Z. P/DOCE (epirubicin or doxorubicin, vincristine, cyclophosphamide, and prednisone).
- 173. (New) A method of treating a subject with a B-cell malignancy, the method comprising administering to the subject a therapeutically effective dose of a composition comprising a monomeric cytotoxic drug derivative/anti-CD22 antibody conjugate, wherein the anti-CD22 antibody of the monomeric cytotoxic drug derivative/anti-CD22 antibody conjugate comprises a light chain variable region having a sequence set forth in SEQ ID NO:28 and a heavy chain variable region having a sequence set forth in SEQ ID NO:30.

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174. (New) The method of claim 173, wherein the anti-CD22 antibody is selected from a group consisting of a monoclonal antibody, a chimeric antibody, a human antibody, a humanized antibody, a single chain antibody, and a biologically active antibody fragment wherein the biologically active fragment is a Fab, a modified Fab, Fab', F(ab')2 or Fv, or a heavy chain monomer or dimer.

- 175. (New) The method of claim 174, wherein the anti-CD22 antibody is a humanized antibody.
- 176. (New) The method of claim 175, wherein the humanized antibody comprises a variable domain comprising human acceptor framework regions and non-human donor CDRs.
- 177. (New) The method of claim 176, wherein the human acceptor framework regions of the variable domain of the heavy chain of the antibody are based on SEQ ID NOS:21 and 22 and comprise donor residues at positions 1, 28, 48, 72 and 97 in SEQ ID NO:8.
- 178. (New) The method of claim 177, wherein the antibody further comprises donor residues at positions 68 and 70 in SEQ ID NO:8.
- 179. (New) The method of claim 175, wherein the anti-CD22 antibody comprises a variable domain of the light chain comprising a human acceptor framework region based on SEQ ID NOS:17 and 18 and further comprising donor residues at positions 2, 4, 42, 43, 50 and 65.
- 180. (New) The method of claim 179, wherein the anti-CD22 antibody further comprises a donor residue at position 3 in SEQ ID NO:7.
- 181. (New) The method of claim 173, wherein the cytotoxic drug is calicheamicin.
- 182. (New) The method of claim 181, wherein the calicheamicin is gamma calicheamicin or N-acetyl gamma calicheamicin.

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(New) The method of claim 181, wherein the calicheamicin derivative is functionalized

with 3-mercapto-3-methyl butanoyl hydrazide.

(New) The method of claim 173, wherein the therapeutically effective dose of the 184.

composition is administered subcutaneously, intraperitoneally, intravenously, intraarterially,

intramedullarly, intrathecally, transdermally, transcutaneously, intranasally, topically, enterally,

intravaginally, sublingually or rectally.

(New) The method of claim 173, wherein the therapeutically effective dose of the 185.

composition is administered intravenously.

186. (New) The method of claim 173, wherein the subject is a human subject.

(New) The method of claim 173, wherein the B-cell malignancy is a leukemia, a 187.

lymphoma or a Non-Hodgkin's lymphoma.

(New) The method of claim 187, wherein the leukemia expresses cell surface antigen 188.

CD22.

(New) The method of claim 187, wherein the lymphoma expresses cell surface antigen 189.

CD22.

(New) The method of claim 173, comprising administering the therapeutically effective 190.

dose of the composition with one or more bioactive agents.

191. (New) The method of claim 190, wherein the one or more bioactive agents are

antibodies.

(New) The method of claim 191, wherein the antibody is directed against a cell surface 192.

antigen expressed on B-cell malignancies.

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193. (New) The method of claim 192, wherein the antibody directed against cell surface antigens expressed on B-cell malignancies is selected from a group consisting of anti-CD19, anti-CD20 and anti-CD33 antibodies.

- 194. (New) The method of claim 193, wherein the anti-CD20 antibody is rituximab.
- 195. (New) The method of claim 191, wherein the therapeutically effective dose of the composition is administered together with an antibody directed against a cell surface antigen on B-cell malignancies, and optionally comprising one or more combinations of cytotoxic agents as a part of a treatment regimen, wherein the combination of cytotoxic agents is selected from:
  - A. CHOPP (cyclophosphamide, doxorubicin, vincristine, prednisone, and procarbazine);
  - B. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone);
  - C. COP (cyclophosphamide, vincristine, and prednisone);
  - D. CAP-BOP (cyclophosphamide, doxorubicin, procarbazine, bleomycin, vincristine, and prednisone);
  - E. m-BACOD (methotrexate, bleomycin, doxorubicin, cyclophosphamide, vincristine, dexamethasone, and leucovorin);
  - F. ProMACE-MOPP (prednisone, methotrexate, doxorubicin, cyclophosphamide, etoposide, leucovorin, mechloethamine, vincristine, prednisone, and procarbazine);
  - G. ProMACE-CytaBOM (prednisone, methotrexate, doxorubicin, cyclophosphamide, etoposide, leucovorin, cytarabine, bleomycin, and vincristine);
  - H. MACOP-B (methotrexate, doxorubicin, cyclophosphamide, vincristine, fixed dose prednisone, bleomycin, and leucovorin);
  - I. MOPP (mechloethamine, vincristine, prednisone, and procarbazine);
  - J. ABVD (adriamycin/doxorubicin, bleomycin, vinblastine, and dacarbazine);
  - K. MOPP (mechloethamine, vincristine, prednisone, and procarbazine) alternating with ABV (adriamycin/doxorubicin, bleomycin, and vinblastine);
  - L. MOPP(mechloethamine, vincristine, prednisone, and procarbazine) alternating with ABVD (adriamycin/doxorubicin, bleomycin, vinblastine, and dacarbazine);
  - M. ChIVPP (chlorambucil, vinblastine, procarbazine, and prednisone);
  - N. IMVP-16 (ifosfamide, methotrexate, and etoposide);

- O. MIME (methyl-gag, ifosfamide, methotrexate, and etoposide);
- P. DHAP (dexamethasone, high-dose cytarabine and cisplatin);
- Q. ESHAP (etoposide, methylpredisolone, high-dose cytarabine, and cisplatin);
- R. CEPP(B) (cyclophosphamide, etoposide, procarbazine, prednisone, and bleomycin);
- S. CAMP (lomustine, mitoxantrone, cytarabine, and prednisone);
- T. CVP-1 (cyclophosphamide, vincristine, and prednisone). ESHOP (etoposide, methylpredisolone, high-dose cytarabine, vincristine and cisplatin);
- U. ESHOP (etoposide, methylpredisolone, high-dose cytarabine, vincristine and cisplatin);
- V. EPOCH (etoposide, vincristine, and doxorubicin for 96 hours with bolus doses of cyclophosphamide and oral prednisone);
- W. ICE (ifosfamide, cyclophosphamide, and etoposide);
- X. CEPP(B) (cyclophosphamide, etoposide, procarbazine, prednisone, and bleomycin);
- Y. CHOP-B. (cyclophosphamide, doxorubicin, vincristine, prednisone, and bleomycin); and
- Z. P/DOCE (epirubicin or doxorubicin, vincristine, cyclophosphamide, and prednisone).
- 196. (New) A method of treating a subject with a B-cell malignancy, the method comprising administering to the subject a therapeutically effective dose of a composition comprising a monomeric cytotoxic drug derivative/anti-CD22 antibody conjugate, wherein the anti-CD22 antibody of the monomeric cytotoxic drug derivative/anti-CD22 antibody conjugate comprises SEQ ID NO:1 for CDR-H1, SEQ ID NO: 2 or SEQ ID NO:13 or SEQ ID NO:15 or SEQ ID NO:16 or residues 50-65 of SEQ ID NO:27 for CDR-H2, SEQ ID NO:3 for CDR-H3, SEQ ID NO:4 for CDR-L1, SEQ ID NO:5 for CDR-L2, and SEQ ID NO:6 for CDR-L3.
- 197. (New) The method of claim 196, wherein the anti-CD22 antibody is selected from a group consisting of a monoclonal antibody, a chimeric antibody, a human antibody, a humanized antibody, a single chain antibody, and a biologically active antibody fragment wherein the biologically active fragment is a Fab, a modified Fab, Fab', F(ab')2 or Fv, or a heavy chain monomer or dimer.

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198. (New) The method of claim 197, wherein the anti-CD22 antibody is a humanized

antibody.

199. (New) The method of claim 198, wherein the humanized antibody comprises a variable

domain comprising human acceptor framework regions and non-human donor CDRs.

200. (New) The method of claim 199, wherein the human acceptor framework regions of the

variable domain of the heavy chain of the antibody are based on SEQ ID NOS:21 and 22 and

comprise donor residues at positions 1, 28, 48, 72 and 97 in SEQ ID NO:8.

201. (New) The method of claim 200, wherein the antibody further comprises donor residues

at positions 68 and 70 in SEQ ID NO:8.

202. (New) The method of claim 198, wherein the anti-CD22 antibody comprises a variable

domain of the light chain comprising a human acceptor framework region based on SEQ ID

NOS:17 and 18 and further comprising donor residues at positions 2, 4, 42, 43, 50 and 65.

203. (New) The method of claim 202, wherein the anti-CD22 antibody further comprises a

donor residue at position 3 in SEQ ID NO:7.

204. (New) The method of claim 196, wherein the cytotoxic drug is calicheamicin.

205. (New) The method of claim 204, wherein the calicheamicin is gamma calicheamicin or

N-acetyl gamma calicheamicin.

206. (New) The method of claim 204, wherein the calicheamicin derivative is functionalized

with 3-mercapto-3-methyl butanoyl hydrazide.

207. (New) The method of claim 196, wherein the therapeutically effective dose of the

composition is administered subcutaneously, intraperitoneally, intravenously, intraarterially,

intramedullarly, intrathecally, transdermally, transcutaneously, intranasally, topically, enterally,

intravaginally, sublingually or rectally.

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208. (New) The method of claim 196, wherein the therapeutically effective dose of the

composition is administered intravenously.

209. (New) The method of claim 196, wherein the subject is a human subject.

210. (New) The method of claim 196, wherein the B-cell malignancy is a leukemia, a

lymphoma or a Non-Hodgkin's lymphoma.

211. (New) The method of claim 210, wherein the leukemia expresses cell surface antigen

CD22.

212. (New) The method of claim 210, wherein the lymphoma expresses cell surface antigen

CD22.

213. (New) The method of claim 196, comprising administering the therapeutically effective

dose of the composition with one or more bioactive agents.

214. (New) The method of claim 213, wherein the one or more bioactive agents are

antibodies.

215. (New) The method of claim 214, wherein the antibody is directed against a cell surface

antigen expressed on B-cell malignancies.

216. (New) The method of claim 215, wherein the antibody directed against cell surface

antigens expressed on B-cell malignancies is selected from a group consisting of anti-CD19,

anti-CD20 and anti-CD33 antibodies.

217. (New) The method of claim 216, wherein the anti-CD20 antibody is rituximab.

218. (New) The method of claim 214, wherein the therapeutically effective dose of the

composition is administered together with an antibody directed against a cell surface antigen on

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B-cell malignancies, and optionally comprising one or more combinations of cytotoxic agents as a part of a treatment regimen, wherein the combination of cytotoxic agents is selected from:

- A. CHOPP (cyclophosphamide, doxorubicin, vincristine, prednisone, and procarbazine);
- B. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone);
- C. COP (cyclophosphamide, vincristine, and prednisone);
- D. CAP-BOP (cyclophosphamide, doxorubicin, procarbazine, bleomycin, vincristine, and prednisone);
- E. m-BACOD (methotrexate, bleomycin, doxorubicin, cyclophosphamide, vincristine, dexamethasone, and leucovorin);
- F. ProMACE-MOPP (prednisone, methotrexate, doxorubicin, cyclophosphamide, etoposide, leucovorin, mechloethamine, vincristine, prednisone, and procarbazine);
- G. ProMACE-CytaBOM (prednisone, methotrexate, doxorubicin, cyclophosphamide, etoposide, leucovorin, cytarabine, bleomycin, and vincristine);
- H. MACOP-B (methotrexate, doxorubicin, cyclophosphamide, vincristine, fixed dose prednisone, bleomycin, and leucovorin);
- 1. MOPP (mechloethamine, vincristine, prednisone, and procarbazine);
- J. ABVD (adriamycin/doxorubicin, bleomycin, vinblastine, and dacarbazine);
- K. MOPP (mechloethamine, vincristine, prednisone, and procarbazine) alternating with ABV (adriamycin/doxorubicin, bleomycin, and vinblastine);
- L. MOPP(mechloethamine, vincristine, prednisone, and procarbazine) alternating with ABVD (adriamycin/doxorubicin, bleomycin, vinblastine, and dacarbazine);
- M. ChIVPP (chlorambucil, vinblastine, procarbazine, and prednisone);
- N. IMVP-16 (ifosfamide, methotrexate, and etoposide);
- O. MIME (methyl-gag, ifosfamide, methotrexate, and etoposide);
- P. DHAP (dexamethasone, high-dose cytarabine and cisplatin);
- Q. ESHAP (etoposide, methylpredisolone, high-dose cytarabine, and cisplatin);
- R. CEPP(B) (cyclophosphamide, etoposide, procarbazine, prednisone, and bleomycin);
- S. CAMP (lomustine, mitoxantrone, cytarabine, and prednisone);
- T. CVP-1 (cyclophosphamide, vincristine, and prednisone). ESHOP (etoposide, methylpredisolone, high-dose cytarabine, vincristine and cisplatin);
- U. ESHOP (etoposide, methylpredisolone, high-dose cytarabine, vincristine and cisplatin);
- V. EPOCH (etoposide, vincristine, and doxorubicin for 96 hours with bolus doses of cyclophosphamide and oral prednisone);

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- W. ICE (ifosfamide, cyclophosphamide, and etoposide);
- X. CEPP(B) (cyclophosphamide, etoposide, procarbazine, prednisone, and bleomycin);
- Y. CHOP-B. (cyclophosphamide, doxorubicin, vincristine, prednisone, and bleomycin); and
- Z. P/DOCE (epirubicin or doxorubicin, vincristine, cyclophosphamide, and prednisone).
- 219. (New) A method of treating a subject with a B-cell malignancy, the method comprising administering to the subject a therapeutically effective dose of a composition comprising a monomeric cytotoxic drug derivative/anti-CD22 antibody conjugate, wherein the anti-CD22 antibody of the monomeric cytotoxic drug derivative/anti-CD22 antibody conjugate comprises a light chain variable region having a sequence set forth in SEQ ID NO:7 and a heavy chain variable region having a sequence set forth in SEQ ID NO:8.
- 220. (New) The method of claim 219, wherein the anti-CD22 antibody is selected from a group consisting of a monoclonal antibody, a chimeric antibody, a human antibody, a humanized antibody, a single chain antibody, and a biologically active antibody fragment wherein the biologically active fragment is a Fab, a modified Fab, Fab', F(ab')2 or Fv, or a heavy chain monomer or dimer.
- 221. (New) The method of claim 220, wherein the anti-CD22 antibody is a chimeric antibody.
- 222. (New) The monomeric cytotoxic drug derivative/carrier conjugate of claim 220, wherein the humanized antibody comprises a variable domain comprising human acceptor framework regions and non-human donor CDRs.
- 223. (New) The method of claim 222, wherein the human acceptor framework regions of the variable domain of the heavy chain of the antibody are based on SEQ ID NOS:21 and 22 and comprise donor residues at positions 1, 28, 48, 72 and 97 in SEQ ID NO:8.
- 224. (New) The method of claim 223, wherein the antibody further comprises donor residues at positions 68 and 70 in SEQ ID NO:8.

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225. (New) The method of claim 220, wherein the anti-CD22 antibody comprises a variable domain of the light chain comprising a human acceptor framework region based on SEQ ID

NOS:17 and 18 and further comprising donor residues at positions 2, 4, 42, 43, 50 and 65.

226. (New) The method of claim 225, wherein the CDR-grafted anti-CD22 antibody further

comprises a donor residue at position 3 in SEQ ID NO:7.

227. (New) The method of claim 219, wherein the cytotoxic drug is calicheamicin.

228. (New) The method of claim 227, wherein the calicheamicin is gamma calicheamicin or

N-acetyl gamma calicheamicin.

229. (New) The method of claim 227, wherein the calicheamicin derivative is functionalized

with 3-mercapto-3-methyl butanoyl hydrazide.

230. (New) The method of claim 219, wherein the therapeutically effective dose of the

composition is administered subcutaneously, intraperitoneally, intravenously, intraarterially,

intramedullarly, intrathecally, transdermally, transcutaneously, intranasally, topically, enterally,

intravaginally, sublingually or rectally.

231. (New) The method of claim 230, wherein the therapeutically effective dose of the

composition is administered intravenously.

232. (New) The method of claim 219, wherein the subject is a human subject.

233. (New) The method of claim 219, wherein the B-cell malignancy is a leukemia, a

lymphoma or a Non-Hodgkin's lymphoma.

234. (New) The method of claim 233, wherein the leukemia expresses cell surface antigen

CD22.

235. (New) The method of claim 233, wherein the lymphoma expresses cell surface antigen

CD22.

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236. (New) The method of claim 219, comprising administering the therapeutically effective

dose of the composition of the monomeric cytotoxic drug derivative/anti-CD22-antibody

conjugate with one or more bioactive agents.

237. (New) The method of claim 236, wherein the one or more bioactive agents are

antibodies.

238. (New) The method of claim 237, wherein the antibody is directed against a cell surface

antigen expressed on B-cell malignancies.

239. (New) The method of claim 238, wherein the antibody directed against cell surface

antigens expressed on B-cell malignancies is selected from a group consisting of anti-CD19,

anti-CD20 and anti-CD33 antibodies.

240. (New) The method of claim 239, wherein the anti-CD20 antibody is rituximab.

241. (New) The method of claim 237, wherein the therapeutically effective dose of the

composition is administered together with an antibody directed against a cell surface antigen on

B-cell malignancies, and optionally comprising one or more combinations of cytotoxic agents as

a part of a treatment regimen, wherein the combination of cytotoxic agents is selected from:

A. CHOPP (cyclophosphamide, doxorubicin, vincristine, prednisone, and procarbazine);

B. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone);

C. COP (cyclophosphamide, vincristine, and prednisone);

D. CAP-BOP (cyclophosphamide, doxorubicin, procarbazine, bleomycin, vincristine, and

prednisone);

E. m-BACOD (methotrexate, bleomycin, doxorubicin, cyclophosphamide, vincristine,

dexamethasone, and leucovorin);

F. ProMACE-MOPP (prednisone, methotrexate, doxorubicin, cyclophosphamide,

etoposide, leucovorin, mechloethamine, vincristine, prednisone, and procarbazine);

G. ProMACE-CytaBOM (prednisone, methotrexate, doxorubicin, cyclophosphamide,

etoposide, leucovorin, cytarabine, bleomycin, and vincristine);

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- H. MACOP-B (methotrexate, doxorubicin, cyclophosphamide, vincristine, fixed dose prednisone, bleomycin, and leucovorin);
- I. MOPP (mechloethamine, vincristine, prednisone, and procarbazine);
- J. ABVD (adriamycin/doxorubicin, bleomycin, vinblastine, and dacarbazine);
- K. MOPP (mechloethamine, vincristine, prednisone, and procarbazine) alternating with ABV (adriamycin/doxorubicin, bleomycin, and vinblastine);
- L. MOPP(mechloethamine, vincristine, prednisone, and procarbazine) alternating with ABVD (adriamycin/doxorubicin, bleomycin, vinblastine, and dacarbazine);
- M. ChIVPP (chlorambucil, vinblastine, procarbazine, and prednisone);
- N. IMVP-16 (ifosfamide, methotrexate, and etoposide);
- O. MIME (methyl-gag, ifosfamide, methotrexate, and etoposide);
- P. DHAP (dexamethasone, high-dose cytarabine and cisplatin);
- Q. ESHAP (etoposide, methylpredisolone, high-dose cytarabine, and cisplatin);
- R. CEPP(B) (cyclophosphamide, etoposide, procarbazine, prednisone, and bleomycin);
- S. CAMP (lomustine, mitoxantrone, cytarabine, and prednisone);
- T. CVP-1 (cyclophosphamide, vincristine, and prednisone). ESHOP (etoposide, methylpredisolone, high-dose cytarabine, vincristine and cisplatin);
- U. ESHOP (etoposide, methylpredisolone, high-dose cytarabine, vincristine and cisplatin);
- V. EPOCH (etoposide, vincristine, and doxorubicin for 96 hours with bolus doses of cyclophosphamide and oral prednisone);
- W. ICE (ifosfamide, cyclophosphamide, and etoposide);
- X. CEPP(B) (cyclophosphamide, etoposide, procarbazine, prednisone, and bleomycin);
- Y. CHOP-B. (cyclophosphamide, doxorubicin, vincristine, prednisone, and bleomycin); and
- Z. P/DOCE (epirubicin or doxorubicin, vincristine, cyclophosphamide, and prednisone).
- 242. (New) A method of treating a subject with aggressive lymphomas comprising administering to the subject a patient in need of said treatment a therapeutically effective dose of a composition comprising a monomeric calicheamicin derivative-anti-CD22-antibody conjugate together with one or more bioactive agents, wherein the monomeric calicheamicin derivative-anti-CD22 antibody conjugate comprises a calicheamicin derivative functionalized with 3-mercapto-3-methyl butanoyl hydrazide and an anti-CD22 antibody comprising SEQ ID NO:1 for CDR-H1, SEQ ID NO: 2 or SEQ ID NO:13 or SEQ ID NO:15 or SEQ ID NO:16 or

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residues 50-65 of SEQ ID NO:27 for CDR-H2, SEQ ID NO:3 for CDR-H3, SEQ ID NO:4 for

CDR-L1, SEQ ID NO:5 for CDR-L2, and SEQ ID NO:6 for CDR-L3.

243. (New) The method of claim 242, wherein the anti-CD22 antibody comprises a variable

domain comprising human acceptor framework regions and non-human donor CDRs.

244. (New) The method of claim 243, wherein the human acceptor framework regions of the

variable domain of the heavy chain of the antibody are based on SEQ ID NOS:21 and 22 and

comprise donor residues at positions 1, 28, 48, 72 and 97 in SEQ ID NO:8.

245. (New) The method of claim 244, wherein the antibody further comprises donor residues

at positions 68 and 70 in SEQ ID NO:8.

246. (New) The method of claim 242, wherein the anti-CD22 antibody comprises a variable

domain of the light chain comprising a human acceptor framework region based on SEQ ID

NOS:17 and 18 and further comprising donor residues at positions 2, 4, 42, 43, 50 and 65.

247. (New) The method of claim 246, wherein the anti-CD22 antibody further comprises a

donor residue at position 3 in SEQ ID NO:7.

248. (New) The method of claim 242, wherein the one or more bioactive agents are

antibodies.

249. (New) The method of claim 248, wherein the antibody is directed against a cell surface

antigen expressed on B-cell malignancies.

250. (New) The method of claim 249, wherein the antibody directed against cell surface

antigens expressed on B-cell malignancies is selected from a group consisting of anti-CD19,

anti-CD20 and anti-CD33 antibodies.

251. (New) The method of claim 250, wherein the anti-CD20 antibody is rituximab.

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252. (New) The method of claim 242, wherein the anti-CD22 antibody comprises a variable domain comprising human acceptor framework regions and non-human donor CDRs.

- 253. (New) The method of claim 252, wherein the human acceptor framework regions of the variable domain of the heavy chain of the antibody are based on SEQ ID NOS:21 and 22 and comprise donor residues at positions 1, 28, 48, 72 and 97 in SEQ ID NO:8.
- 254. (New) The method of claim 253, wherein the antibody further comprises donor residues at positions 68 and 70 in SEQ ID NO:8.
- 255. (New) The method of claim 242, wherein the anti-CD22 antibody comprises a variable domain of the light chain comprising a human acceptor framework region based on SEQ ID NOS:17 and 18 and further comprising donor residues at positions 2, 4, 42, 43, 50 and 65.
- 256. (New) The method of claim 255, wherein the anti-CD22 antibody further comprises a donor residue at position 3 in SEQ ID NO:7.